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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JOIKE, MICHELE K	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,199	BUDWORTH ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in the reply filed on December 9, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claim 16 refers to a plurality of binding partners and claim 17 claims a plurality of binding partners and a plurality of nucleic acid expression vectors introduced into a cell, neither of which is supported by the disclosure.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figure 1 contains a nucleic acid sequence and an amino acid sequence that need sequence identifiers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 9, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronan.

Applicants claim a method for obtaining *in vivo* binding partners of a protein comprising obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating the complex from the extract. The fusion protein is a heterologous protein, and there is a cleavage site between the protein of interest and the post-translational sequence. The method also includes identifying binding partners, including a plurality of binding partners. The method can also be performed by transforming a cell with a vector encoding the fusion protein.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7) teaches a method for obtaining *in vivo* binding partners of a protein comprising obtaining a transformed host cell (bacteria, yeast, other fungi, plant, insect or mammalian) and expressing a fusion protein comprising a protein of interest and a

post-translation biotination sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract. The fusion protein is a heterologous protein, and there is a cleavage site between the protein of interest and the post-translation biotination sequence. The method also includes identifying binding partners, indicating that more than one binding partner is identified. The method can also be performed by transforming a cell with a vector encoding the fusion protein. As such, Cronan anticipates each one of these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4-9 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view of Rigaut et al.

Applicants claim the method described above further limited by the fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7,

Claims 1, 2 and 7) teaches all of the limitations as described above. However, it does not teach affinity tagging the fusion protein, or cleaving the protein of interest from the post-translational modification sequence prior to identifying binding partners of the protein of interest. Rigaut et al (Nature Biotech, 17: 1030-1032, 1999, see entire article, specifically Figure 1) teach a transformed yeast cell with a fusion protein comprising a heterologous protein with two affinity tags, a *S. aureus* protein A IgG binding domain and a calmodulin binding peptide, as well as a TEV cleavage site. They also teach making a cell extract and purification of the protein of interest. They also teach that the target protein is cleaved before purification and electrophoresis. Therefore, the target protein is cleaved from the post-translational modification sequence prior to identifying binding partners of the target protein.

The ordinary skilled artisan, desiring to perform a method for obtaining *in vivo* binding partners of a protein comprising obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract with the fusion protein being a heterologous protein, and there is a cleavage site between the protein of interest and the post-translational sequence, and to use a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step, would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein

comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract with the teachings of Rigaut et al, of a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step. There would be motivation to combine the teachings because affinity tagging allows for rapid purification of proteins, especially heteromeric complexes. It would have been obvious to one of ordinary skill in the art to use affinity tagging for purification because these affinity tags do not impair function and allow for efficient recovery. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view of Rigaut et al and in further view of Luo et al.

Applicants claim the method described above further limited by use of a mammalian host cell.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7) and Rigaut et al (Nature Biotech, 17: 1030-1032, 1999, see entire article, specifically Figure 1) teach all of the limitations as described above. However,

they do not teach the use of a mammalian host cell. Luo et al (U.S. 6,114,111, specifically Background, 4th paragraph) teach the use of a mammalian cell containing a fusion protein.

The ordinary skilled artisan, desiring to perform the method described above in mammalian cells would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract with the teachings of Rigaut et al, of a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step and Luo et al of use of a mammalian cell containing a fusion protein. There would be motivation to combine the teachings because Cronan teaches that there are a large number of available and well-known host cells, including mammalian cells available to perform this method and Luo et al teach mammalian cells are desirable for fusion proteins because mammalian cells have different post-translational modification systems than yeast. It would have been obvious to one of ordinary skill in the art to use mammalian cells because they are they can be tested under a variety of experimental conditions that may affect intracellular protein-protein interactions. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be

considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view of Rigaut et al, Luo et al, and in further view of Fields.

Applicants claim the method described above further limited by a plurality of potential binding partners encoded by a plurality of nucleic acid expression vectors.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7), Rigaut et al (Nature Biotech, 17: 1030-1032, 1999, see entire article, specifically Figure 1) and Luo et al (U.S. 6,114,111, specifically Background, 4th paragraph) teach all of the limitations as described above. However, they do not teach a plurality of potential binding partners encoded by a plurality of nucleic acid expression vectors. Fields (U.S. 5,283,173, specifically column 3, paragraph 2) teaches a library of cDNA plasmids for a yeast two-hybrid assay.

The ordinary skilled artisan, desiring to perform the method described above with a plurality of nucleic acid expression vectors would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract with the teachings of Rigaut et al, of a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding

domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step and the teachings of Luo et al of use of a mammalian cell containing a fusion protein with Fields teaching a library of cDNA plasmids. There would be motivation to combine the teachings because Fields teaches that an advantage of producing a multiplicity of proteins is that they can be simultaneously tested for interaction. It would have been obvious to one of ordinary skill in the art to use a plurality of nucleic acid expression vectors because they can produce many binding partners and be used to test affinity reagents. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER